A Retrospective Comparison Of Platelet Indices For Diagnosing Infected Nonunion

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Abstract

Background: Previous studies have been conducted to evaluate the diagnostic values of platelet indices in some infectious diseases. However, the predictive values of platelet indices for infected nonunion have not yet been evaluated. The purpose of this study was to assess the diagnostic performance of platelet indices in infected nonunion.

Methods: This study was performed retrospectively on patients who underwent primary fracture nonunion revision surgeries from January 2016 to December 2021. 297 patients with 96 infected nonunion (group A) and 201 aseptic nonunion (group B) who met our inclusion criteria were included. Receiver Operator Characteristic (ROC) curve, sensitivity, and specificity of preoperative clinical parameters were analyzed and compared.

Results: The demographic characteristics were similar and had no significant difference between two groups. Compared with group B, the levels of WBC, CRP, ESR, plasma fibrinogen, plasma D-dimer, PC, PCT, and PC/MPV were significantly higher, but the levels of MPV and PDW were significantly lower in group A ($p < 0.05$). ROC curves showed that PC/MPV and plasma fibrinogen outperformed the other coagulation indicators, with areas under the curve of 0.801 and 0.807, respectively. The multiple tests of ESR, plasma fibrinogen and PC/MPV had good sensitivity and specificity for the diagnosis of infected nonunion, and the diagnostic values of PC/MP was better than ESR and plasma fibrinogen in the subgroup.

Conclusions: Our study demonstrates that the diagnostic performance of coagulation indicators, plasma fibrinogen and PC/MPV, are high and they can increase the accuracy of infected nonunion diagnosis.

Introduction

Open reduction and internal fixation (ORIF) for fractures has been one of the most successful surgeries during the last century. Patients with fractures can achieve relief of pain and functional recovery after ORIF. However, infected nonunion, which is associated with higher hospitalization costs, longer treatment course and even higher morbidity and mortality rates than the primary procedure, is one of the most disruptive and complex complications following ORIF[1, 2]. It is a huge economic burden not only for the individual patient but also for the global healthcare system. Accurate differentiation between infected nonunion and aseptic nonunion is important for planning and implementing treatment regimens. As traditional inflammatory markers, white blood cell (WBC), C-reactive protein (CRP) and the erythrocyte sedimentation rate (ESR) are still the most commonly used indicators for detecting infected nonunion with the advantages of simplicity, accessibility, and short waiting time[3]. However, with the typical clinical manifestations of infection decreasing and the quiescent infection rising, the diagnostic performances of WBC, CRP and ESR tests are not always satisfactory[4–6]. Considering lacking absolutely reliable indicators, the diagnosis and treatment of infected nonunion remains challenging[6, 7]. Therefore, finding more potential novel blood markers is quite important for community-level medical institutions.

Many studies have indicated a close association between coagulation and inflammation[8–11]. Several coagulation-related parameters, such as fibrinogen, D-dimer and platelet count have been demonstrated as promising diagnostic markers of infection[12, 13]. Inspired by this, many scholars have focused on exploring the potential values of coagulation-related parameters for diagnosing orthopaedic infections and have obtained positive outcomes that fibrinogen, D-dimer and PC are useful in reaching or refuting the diagnosis of periprosthetic joint infection (PJI)[14–18]. Moreover, past studies have indicated that D-dimer and fibrinogen could be potential diagnostic markers for infected nonunion[19, 20]. However, the sample sizes of the studies were not enough large and there is no related study about the accuracy of platelet indices including platelet count (PC), plateletcrit (PCT), mean platelet volume (MPV), platelet distribution width (PDW), and PC/MPV in diagnosing infected nonunion after ORIF.

Therefore, we aim to review more samples to evaluate the accuracy of the easily accessible and routinely available established inflammatory biomarkers (WBC, CRP, and ESR) and also routinely available coagulation-related parameters (fibrinogen, D-dimer and platelet indices) in the diagnosis of infected nonunion after ORIF. In addition, a comparison among coagulation-related parameters fibrinogen, D-dimer and platelet indices (PC, PCT, MPV, PDW, and PC/MPV) was done to find the coagulation-related inflammatory marker with the best performance in the diagnosis of infected nonunion after ORIF.

Methods

Study design and participants. This study was approved by the ethical committee of our institution, and experimental procedures were conducted following the declaration of Helsinki. All patients provided written informed consent before operation. From January 2016 to December 2021, a total of 384 patients who underwent fracture nonunion revision surgeries were included as our initial patients. Patients who had undergone refixation surgeries (n = 16) were excluded because its complex source of pathogens and uncertain duration of infection. And patients with insufficient data (n = 9) and antibiotic use (n = 8) were excluded. In order to exclude the possibility of bias, 54 patients with comorbidities, which included venous thrombosis (n = 20), cardiovascular and cerebrovascular diseases (n = 11), malignancy (n = 4), liver or kidney failure (n = 4), diseases of the blood system (n = 3) and infection in a site other than a fracture (n = 12), were analyzed separately. Ultimately, 297 patients were included in the research regimen.

We defined nonunion as an arrest in the biologic fracture repair process, as seen on imaging, for three consecutive months with a minimum of nine months between the index procedure and diagnosis[21]. The AO/ASIF criteria were used to define infected nonunion[6]. To identify an infection, intraoperatively, multiple gross tissue specimens (≥ 5 samples) were cultured. A positive diagnosis of infection was made if the same organism was grown in at least 2 cultures of the intraoperative sample. Based on the results of their intraoperative cultures, the patient population was divided into two groups: 96 in Group A (infected nonunion) and 201 in Group B (aseptic nonunion).

Demographic features and blood biomarkers. The basic information of all patients was acquired from the electronic medical record system of the institution, including age, gender, Body mass index (BMI), and the

involved location. The patients were forbidden to eat and drink in the early morning of the day after hospitalization, and the patients' fasting venous blood samples were collected routinely. Within 1–2 h, the blood samples were sent to the Medical Laboratory Center for routine examination. The levels of WBC, CRP, ESR, plasma fibrinogen, plasma D-dimer, PC, PCT, MPV, PDW, and PC/MPV were analyzed. Antibiotic use for the participants was delayed at least 2 weeks until after intraoperative specimens were collected.

Statistical analysis. All the statistical analyses were performed with the statistical software STATA version 18.0 (SPSS Inc., Chicago, IL, USA). Categorical variables were expressed as frequencies and percentages, and analyzed by Pearson χ2 test or Fisher exact test. Kolmogorov-Smirnov (K-S) test was used to identify data as normally distributed variables or non-normally distributed data. Continuous normally distributed variables were presented as mean ± SD (standard deviation), and analyzed by Student's t-tests. Non-normally distributed data was shown as median (IQR), and Mann-Whitney U test was used to analyze numerical variables with non-normal distribution or unequal variance. All differences were considered significant at a value of $P < 0.05$. Patient characteristics were shown in Table 1. There was no significant difference in age, gender, BMI between groups. Receiver operating characteristic curves (ROC) were used to evaluate the value of each biomarker in predicting fracture infected nonunion before revision surgeries. The area under the curve (AUC), 95% confidence interval (CI), and sensitivity and specificity of different markers were determined using the working subject curve. The Youden index (J = [sensitivity + specificity] – 1) was used to identify the optimal predictive cut-offs for the tested markers. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of each test were calculated. AUC scores are typically considered excellent if they exceed 0.9, with an AUC of 0.8 to 0.9 representing a good test, with an AUC of 0.7 to 0.8 representing a fair test, with an AUC of 0.6–0.7 representing a poor test and an AUC of under 0.6 representing no discriminatory capacity.

Table 1
Patient characteristics

	Group A (n = 96)	Group B (n = 201)	*P*-value
Age (year, mean ± SD)	47.2 ± 14.8	45.4 ± 13.6	0.277*
Number of women	16/80(16.7%)	54/147(26.9%)	0.058†
BMI (kg/m^2, mean ± SD)	24.4 ± 2.3	24.7 ± 2.9	0.751*
Position (upper limb)	9/87 (10.3%)	29/172 (14.4%)	0.267†
Group A = infected nonunion; Group B = aseptic nonunion.			
*Independent-samples *t*-test.			
† Chi-squared test (linear by linear).			
BMI = body mass index; $P < 0.05$ indicates statistical significance.			

Results

The levels of WBC, CRP, ESR, plasma fibrinogen, plasma D-dimer, PC, PCT, and PC/MPV were significantly higher in group infected nonunion than in group aseptic nonunion ($P < 0.05$). On the contrary, the levels of MPV and PDW were significantly lower in group infected nonunion than in group aseptic nonunion ($P < 0.05$). The laboratory ranges for the tested markers are shown in Table 2.

Table 2
Comparison of the tested markers in the two groups

	Group A (n = 96)	Group B (n = 201)	*P*-value
WBC (10^9/μL)			
Median	7.0	6.1	< 0.001*
P25, P75	5.8 ~ 8.6	5.3 ~ 7.4	
PC (10^9/L)			< 0.001*
Median	303.0	209.0	
P25, P75	221.8 ~ 404.0	178.5 ~ 259.5	
PCT (%)			< 0.001*
Median	0.32	0.23	
P25, P75	0.25 ~ 0.38	0.19 ~ 0.27	
PDW(%)			< 0.001*
Median	15.8	16.0	
P25, P75	15.4 ~ 16.2	15.5 ~ 16.4	
MPV(fl)			0.008*
Median	9.1	10.1	
P25, P75	8.2 ~ 10.2	9.4 ~ 11.6	
PC/MPV			< 0.001*
Median	34.5	20.2	
P25, P75	22.5 ~ 45.1	16.1 ~ 26.6	
CRP (mg/L)			< 0.001*
Median	8.6	3.7	
P25, P75	4.9 ~ 29.7	2.5 ~ 5.4	
ESR (mm/hr)			< 0.001*

Group A = infected nonunion; Group B = aseptic nonunion.

All P-values calculated using Mann-Whitney U test.

*P < 0.05 indicates statistical significance.

WBC, white blood cell; PC, platelet count; PCT, plateletcrit; MPV, mean platelet volume; PDW, platelet distribution width CRP; C-reactive protein; ESR, erythrocyte sedimentation rate.

	Group A (n = 96)	Group B (n = 201)	*P*-value
Median	26.5	8.0	
P25, P75	16.0 ~ 52.5	5.0 ~ 14.0	
Plasma D-dimer (mg/L)			< 0.001*
Median	1.10	0.36	
P25, P75	0.49 ~ 2.85	0.20 ~ 0.75	
Plasma fibrinogen (mg/L)			< 0.001*
Median	3.8	2.6	
P25, P75	2.9 ~ 5.3	2.3 ~ 3.1	
Group A = infected nonunion; Group B = aseptic nonunion.			
All P-values calculated using Mann-Whitney U test.			
*P < 0.05 indicates statistical significance.			
WBC, white blood cell; PC, platelet count; PCT, plateletcrit; MPV, mean platelet volume; PDW, platelet distribution width CRP; C-reactive protein; ESR, erythrocyte sedimentation rate.			

All tested markers were evaluated and depicted in one receiver operating characteristic curve (Fig. 1). The ROC curves showed that the AUCs (95% confidence interval) of 3 classic inflammatory markers, WBC, CRP, and ESR, were 0.632 (0.562–0.702), 0.774 (0.714–0.833), and 0.848 (0.800-0.896), respectively. The AUCs for coagulation-related tested markers, plasma fibrinogen, plasma D-dimer, PC, PCT, PDW, MPV, and PC/MPV were 0.807 (0.752–0.862), 0.755 (0.696–0.815), 0.769 (0.706–0.833), 0.785 (0.721–0.849), 0.595 (0.528–0.662), 0.722 (0.661–0.783), and 0.801 (0.744–0.858),respectively. The AUCs of these three markers (ESR, plasma fibrinogen, and PC/MPV) ranged from 0.800–0.899, which indicated that they had good diagnostic values for diagnosing infected nonunion. The AUCs for CRP, plasma D-dimer, PC, PCT, and PDW were among 0.700-0.799, indicating fair performances for diagnosing infected nonunion. Nevertheless, the diagnostic accuracy of WBC was poor, and PDW had no discriminatory capacity in diagnosing infected nonunion. Based on the Youden index, the optimal threshold, sensitivity, specificity, PPV, and NPV were 8.05×10^9/L, 38.54, 86.07, 56.92, and 74.57% for WBC; 6.35 mg/L, 67.71, 82.09, 64.36, and 61.22% for CRP; 17.5 mm/h, 72.92, 82.59, 78.26, and 67.44% for ESR; 0.92 mg/L, 60.42, 82.59, 62.37, and 81.37% for plasma D-dimer; 3.35 g/L, 63.54, 84.58, 66.30, and 82.93% for plasma fibrinogen; 294.5×10^9/L, 56.25, 90.05, 72.97,and 81.17% for PC; 0.275%, 70.83, 79.10, 78.26, and 67.44% for PCT; and 15.9%, 54.17, 56.22, 37.14, and 71.97% for PDW; 9.3 fl, 57.29, 75.62, 52.88, and 78.76% for MPV, and 31.7, 58.33, 93.53, and 81.16% for PC/MPV(Table 3).

Table 3
The diagnostic value of tested markers in patients in the two groups.

Variables	AUC (95%CI)	Optimal Cutoff Value	Sensitivity (%)	Specificity(%)	PPV (%)	NPV (%)
WBC	0.632 (0.562–0.702)	8.05×10^9/L	38.54	86.07	56.92	74.57
PC	0.769 (0.706–0.833)	294.5×10^9/L	56.25	90.05	72.97	81.17
PCT	0.785 (0.721–0.849)	0.275%	70.83	79.10	78.26	67.44
PDW	0.595 (0.528–0.662)	15.9%	54.17	56.22	37.14	71.97
MPV	0.722 (0.661–0.783)	9.3 fl	57.29	75.62	52.88	78.76
PC/MPV	0.801 (0.744–0.858)	31.7	58.33	93.53	81.16	82.46
CRP	0.774 (0.714–0.833)	6.35 mg/L	67.71	82.09	64.36	61.22
ESR	0.848 (0.800-0.896)	17.5 mm/h	72.92	82.59	78.26	67.44
Plasma D-dimer	0.755 (0.696–0.815)	0.92 mg/L	60.42	82.59	62.37	81.37

WBC, white blood cell; PC, platelet count; PCT, plateletcrit; MPV, mean platelet volume; PDW, platelet distribution width; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; AUC, areas under the curve; CI, confidence interval; PPV, positive predictive value; NPV, negative predictive value.

Variables	AUC (95%CI)	Optimal Cutoff Value	Sensitivity (%)	Specificity(%)	PPV (%)	NPV (%)
Plasma fibrinogen	0.807 (0.752–0.862)	3.35 g/L	63.54	84.58	66.30	82.93

WBC, white blood cell; PC, platelet count; PCT, plateletcrit; MPV, mean platelet volume; PDW, platelet distribution width; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; AUC, areas under the curve; CI, confidence interval; PPV, positive predictive value; NPV, negative predictive value.

In addition, multiple combinations of plasma fibrinogen, ESR and PC/MPV were performed and their diagnostic values were assessed based on the optimal predictive cutoff values determined by using the Youden index. When using the criteria of PC/MPV 31.7 “or” Plasma fibrinogen 3.35 g/L “or” ESR 17.5 mm/h to detect infected nonunion, the sensitivity (87.50%) was highest. When using the criteria of PC/MPV 31.7 “and” Plasma fibrinogen 3.35 g/L “and” ESR 17.5 mm/h to detect infected nonunion, the specificity (99.00%) was highest (Table 4).

Table 4
The Combinational Diagnostic Values of the Tested Markers

Variables	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
PC/MPV or Plasma fibrinogen	78.13	80.10	65.22	88.46
PC/MPV + Plasma fibrinogen	41.67	98.01	90.91	77.87
PC/MPV or ESR	82.29	77.61	63.71	90.17
PC/MPV + ESR	48.95	98.51	94.00	80.16
Plasma fibrinogen or ESR	84.38	73.63	60.45	90.80
Plasma fibrinogen + ESR	52.08	93.53	79.37	80.34
PC/MPV or Plasma fibrinogen or ESR	87.50	69.15	57.53	92.05
PC/MPV + Plasma fibrinogen + ESR	39.58	99.00	95.00	77.43

PC, platelet count; MPV, mean platelet volume; ESR, erythrocyte sedimentation rate; PPV, positive predictive value; NPV, negative predictive value.

Among 54 patients with coagulation-related comorbidities, there were 31 patients with infected nonunion and 23 patients with aseptic nonunion. Table 5 showed that the diagnostic values of ESR, plasma fibrinogen, and PC/MPV in patients with coagulation-related comorbidities (n = 54), including venous thrombosis (n = 20), cardiovascular and cerebrovascular diseases (n = 11), malignancy (n = 4), liver or kidney failure (n = 4), diseases of the blood system (n = 3) and infection in a site other than a fracture (n = 12) based on the optimal predictive cutoff values determined using Youden's index. PC/MPV was promising for diagnosing infected nonunion in patients with coagulation-related comorbidities (sensitivity

and specificity: 77.41% and 91.30%, respectively, and PPV and NPV: 92.31% and 75.00%, respectively). Plasma fibrinogen was promising for diagnosing infected nonunion in patients with coagulation-related comorbidities (sensitivity and specificity: 64.52% and 73.91%, respectively, and PPV and NPV: 76.92% and 60.71%, respectively). However, the value of ESR was limited for diagnosing infected nonunion in patients with those patients (sensitivity and specificity: 48.39% and 52.17%, respectively, and PPV and NPV: 57.69% and 42.86%, respectively) (Table 5).

Table 5
Diagnostic Values of Tested Markers for Patients with Coagulation-Related Comorbidities

Variables	N (Infected/Aseptic)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Plasma fibrinogen	31/23	48.39	52.17	57.69	42.86
ESR	31/23	64.52	73.91	76.92	60.71
PC/MPV	31/23	77.41	91.30	92.31	75.00

PC, platelet count; MPV, mean platelet volume; ESR, erythrocyte sedimentation rate; PPV, positive predictive value; NPV, negative predictive value.

Discussion

A review of the literature confirmed that our study was the first to use the promising coagulation-related indicators (plasma fibrinogen, plasma D-dimer, PC, PCT, MPV, PDW, and PC/MPV) to differentiate aseptic nonunion and infected nonunion in the same study population. We also evaluated the values of promising coagulation-related indicators and the classic inflammatory markers (WBC, ESR and CRP) for diagnosing infected nonunion. Our data demonstrated that the elevated plasma fibrinogen, PC/MPV and ESR were associated with infected nonunion. And some studies have showed that elevated plasma fibrinogen and ESR performed well for diagnosing infected nonunion, which is similar with the result of this study[19]. Moreover, we assessed the diagnostic values of combining ESR with plasma fibrinogen and PC/MPV. The results indicated that PC/MPV had good performance for diagnosing infected nonunion before revision surgeries. Meanwhile, in subgroup analysis, the value of PC/MPV was better than other markers for diagnosing infected nonunion in patients with coagulation-related comorbidities. In this study, PC/MPV as a traditional coagulation-related indicator may be a practical and cost-efficient biomarker for detecting infected nonunion.

It is well known that inflammation and infection are important regulators of coagulation and fibrinolytic system activity[22, 23]. Considering the easy measurement method by automatic blood counter devices, various studies were conducted to investigate the role of coagulation-related parameters, fibrinogen, D-dimer and platelet indices (PC, PCT, MPV, PDW, and PC/MPV) in the diagnosis of various infectious or inflammatory conditions[24–26]. Until now, numerous studies have evaluated the performances that fibrinogen, D-dimer and platelet indices play in diagnosis of PJI, and most of these studies proved that

fibrinogen, D-dimer and platelet indices were associated with PJI[27–29, 18, 30, 31]. Previous studies have demonstrated that the diagnostic values of plasma fibrinogen and serum D-dimer for diagnosis infected nonunion were good and compared with plasma D-dimer, plasma fibrinogen had better performance in diagnosing infected nonunion, which was consistent with the findings in this study[19, 32]. Based on our data, plasma fibrinogen had the higher AUC (0.807) than plasma D-dimer (0.755). Moreover, we found plasma fibrinogen had a slightly higher sensitivity, specificity, PPV, and NPV compared to plasma D-dimer. Additionally, although some studies have proved that serum D-dimer is superior to plasma D-dimer in diagnosis of PJI[33, 34]. However, we are unaware of studies comparing the diagnostic value of D-dimer levels in plasma or serum sampled from the same patients with infected nonunion. Consequently, high-quality prospective studies that address these research gaps are needed to validate the use of D-dimer as a biomarker for infected nonunion.

Platelet, generated from megakaryocytes, is a part of the natural immune system and rapidly activated during the inflammation process[35]. In bacterial infections, platelets are mechano-scavengers that can collect and bundle microorganisms in a way that supports the leukocyte function, and hence, directly facilitate the host's response to infection[13]. The reason we employed platelets and their corresponding laboratory values (PCT, MPV, PDW), aside from their easily accessible nature, because it has long been known that platelets play a large role in our bodies' innate immune response[36]. However, our study showed that all the AUCs for PC, PCT, MPV, and PDW were less 0.8, which indicated that the values of them in diagnosing infected nonunion were not good. Among them, PC had the highest specificity with 90.05 and NPV with 81.17, but low sensitivity with 56.25. In the presence of inflammation and infection, the platelet production intensifies, and the mean platelet volume drops, and the inverse relationship between of PC and MPV leads to an elevated ratio between these two variables[27]. Paziuk et al.[27] firstly investigated the use of PC/MPV as a diagnostic tool for PJI, and they reported that PC/MPV may be useful in the workup of potential PJI. Tirumala et al.[37] retrospectively compared the PC/MPV values in 538 patients who underwent revision TKA and found PC/MPV can be used with other hematologic and aspirate markers to increase the accuracy of PJI diagnosis in TKA patients. On the contrary, Shang et al.[38] reported that platelet-related markers, such as PC, PCT and PC/MPV have fair diagnostic values for PJI, and no superiority was found when comparing with ESR and CRP. Our results showed that PC/MPV (cut-off: 31.7; AUC 0.801) performed better than other platelet-related markers (< 0.800) and equally to plasma fibrinogen (0.807), but worse than ESR (0.848) in diagnosing infected nonunion. Meanwhile, PC/MPV had the highest specificity (93.53%) and high NPV (82.46) compared with other markers. Furthermore, using three markers (PC/MPV, plasma fibrinogen, ESR) as indicators of infected nonunion incurs no additional cost. Therefore, combined with PC/MPV, plasma fibrinogen, ESR may be promising biomarkers for screening infected nonunion before revision fixation surgeries.

We evaluated these patients with coagulation-related comorbidities separately to indicate the different efficacies of the tested indicators. Our results showed that PC/MPV is useful for diagnosing infected nonunion in patients with coagulation-related comorbidities with a sensitivity of 77.41% and a specificity of 91.3%, which was superior to ESR (with a sensitivity of 64.52% and a specificity of 73.91%) and plasma fibrinogen (with a sensitivity of 48.39% and a specificity of 52.17%).

There were several limitations associated with our study. Firstly, this study pertains to its retrospective nature, which has its own inherent biases, such as selection and information bias. Secondly, although we excluded these patients with antibiotic use in 2 weeks before revision surgeries, which is associated with lower diagnostic laboratory median values. However, detailed information for antibiotic use was not recorded for some patients; this might have affected our results. Thirdly, the kinds of patients with coagulation-related comorbidities were too various and the sample sizes of patients with comorbidities, especially for the patients with venous thrombosis and cardiovascular disease, were too small to evaluate the diagnostic values of tested markers. Therefore, larger-scale, prospective studies, and subgroup analyses are needed to further investigate the value of these biomarkers to predict early infected nonunion.

Conclusion

In summary, all PC/MPV, ESR and plasma fibrinogen levels are significantly high in patients with infected nonunion compared to those with aseptic nonunion. PC/MPV has a high specificity for the diagnosis of infected nonunion. Considering the low cost and easy access of the complete blood tests, the use of PC/MPV as a new tool to facilitate the infected nonunion diagnosis at the suspected time after ORIF sounds promising.

Abbreviations

BMI: body mass index; WBC: white blood cell; PC: platelet count; PCT: plateletcrit; MPV: mean platelet volume; PDW: platelet distribution width; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate. AUC: areas under the curve; CI: confidence interval; PPV: positive predictive value; NPV: negative predictive value; ROC: receiver operator characteristic; ORIF: open reduction and internal fixation; K-S: kolmogorov-smirnov;

Declarations

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Author contributions

Conception and design were the responsibility of Z-W, H-JM, and G-YX. Data collection was the responsibility of Z-W, X-SQ, and Y-XC. Statistical analysis was the responsibility of H-JM and Z-W. Analysis and interpretation were the responsibility of Z-W. Composition of the manuscript was the responsibility of H-JM and Z-W. Revision of the manuscript for important intellectual content and approval of the final draft were done by all authors. G-YX took responsibility for the paper as a whole. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

This study was approved by the ethics committee of Nanjing Drum Tower Hospital, The Affiliated Hospital of Nanjing University Medical School, China (approval no.2021–189). All patients signed an informed consent form approved by the Institutional Review Board.

Consent to Publish

Not applicable

Competing Interests

All the authors declare that there is no conflict of interest.

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Figures

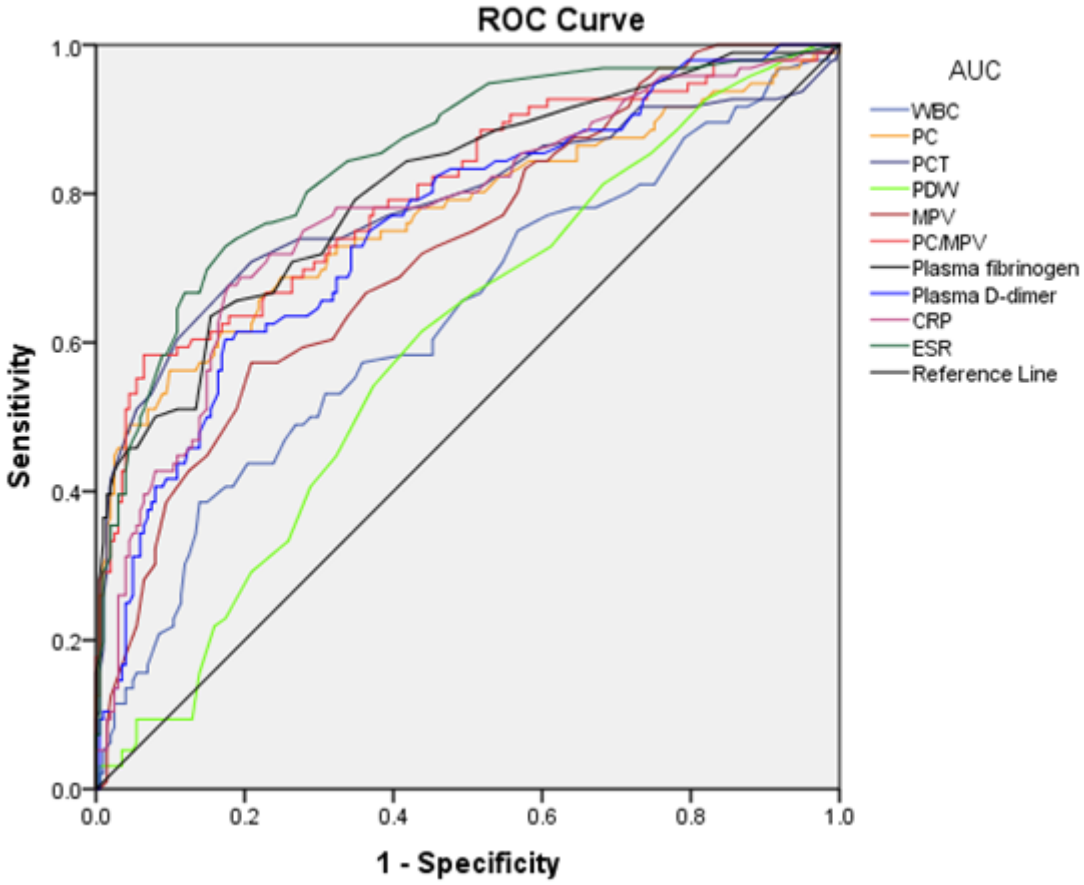

Figure 1

The ROC curves of biomarkers in the diagnosis of infected nonunion. Notes: WBC, white blood cell; PC, platelet count; PCT, plateletcrit; MPV, mean platelet volume; PDW, platelet distribution width; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate.